GAU 1621

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Buchwald, S.L. et al. Examiner: Barts, S.

Application Serial No.: 09/239,024 Art Unit: 1621

Filed: January 27, 1999 **Atty. Docket No.: MTV-009.02**

Title: *Arylation and Vinylation of Activated Carbons*

Assistant Commissioner for Patents
Washington, DC 20231

Certificate of Mailing

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8/24/01 By: Dana Gordon
Date of Signature and Mail Deposit Dana Gordon

Declaration Under 37 CFR § 1.131

Dear Examiner Barts:

As an inventor named on the above-identified application, I hereby declare that the subject matter of rejected claims 1-35 was invented in the United States prior to the effective date, October 16, 1997, of United States Patent 6,057,456.

In support of this Declaration, I attach hereto copies of pages, with their entry dates redacted, from laboratory notebooks maintained by me or one or more of my joint inventors, establishing a reduction to practice of the subject matter of the rejected claims prior to the effective date, October 16, 1997, of United States Patent 6,057,456. Notwithstanding the fact that the entry dates on these pages have been redacted, I hereby declare that these documents establish that a reduction to practice of the subject matter of the rejected claims took place in the United States prior to the effective date, October 16, 1997, of United States Patent 6,057,456.

I hereby declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Stephen L. Buchwald: Stephen L. Buchwald Date: 8/23/01

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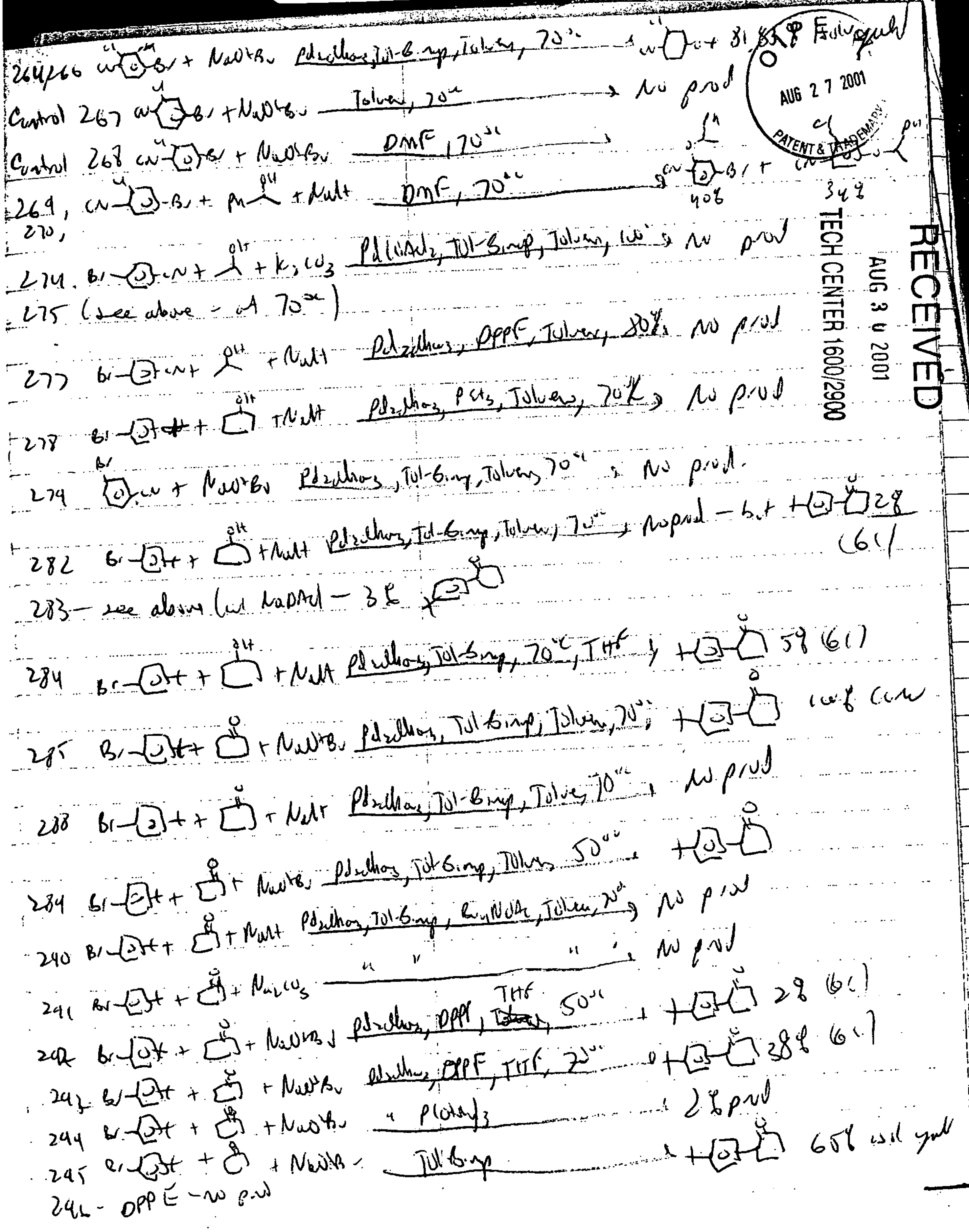
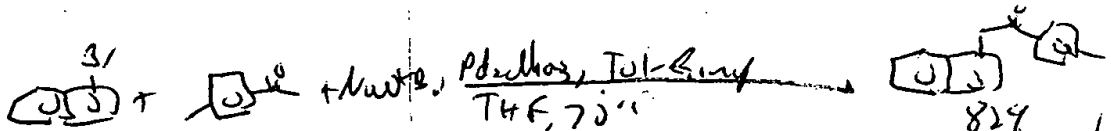
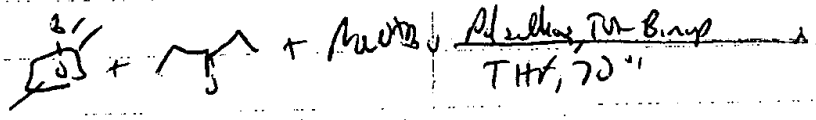
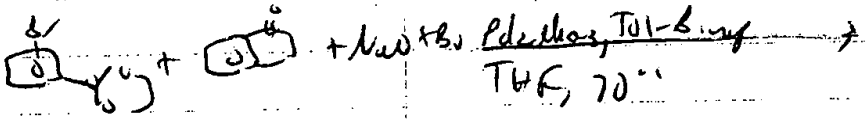
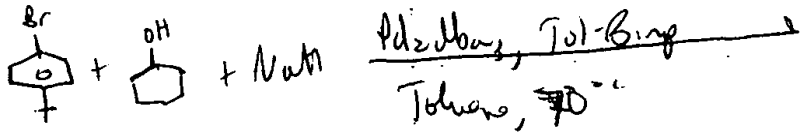
09/239,024



301  82% isol yield

302 

303 



Compound	MW	equiv	mmole	amount	source
t-Butyl bromobenzene	213.12	1.0	0.5	55 µl	
Cyclohexanol	86.13	5.0	2.5	363 µl	
NaH (60%)	23.99	6.0	3.0	120 mg	
$Pd_2(dba)_3$	915.7	0.015	0.0075	6.9 mg	
Tol-Binap	678.79	0.036	0.018	12.2 mg	
Toluene				4 ml	

An oven dried Schlenk flask equipped with a stir bar was charged with NaH, evacuated and back filled with argon. To this was added 2 ml of Toluene and cyclohexanol. The mixture was heated to 70°C for 10 min, at which time t-Butyl bromobenzene, $Pd_2(dba)_3$, Tol-Binap and 1 ml of Toluene were added. The resulting mixture was heated to 70°C while under argon.

11/26/96 - after ~ 15 hrs, took aliquot

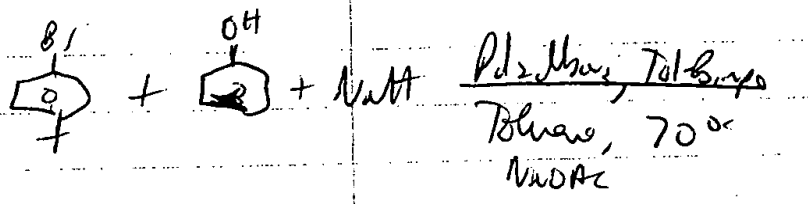
MP 61-II-282-1

87% 

6.4% 

2.7% para, 2.7% 

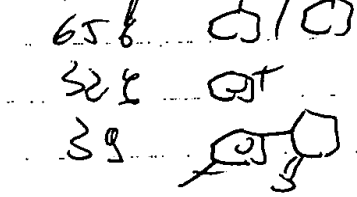
MP 6CMS-II-282-1

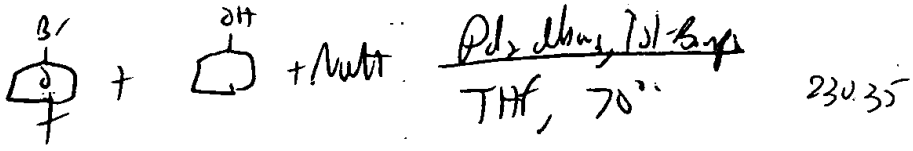


Compound	MW	equiv	mmol	amount
+ Butyl bromobenzene	213.12	1.0	0.5	55 µl
Cyclobutanol	86.13	1.2	0.6	87 µl
NaH (60%)	23.97	2.0	1.0	40 mg
Pd_2dba_3	915.7	0.015	0.0075	6.4 mg
NaOAc	82.03	1.0	0.5	41.0 mg
Tol-Binap	636.74	0.036	0.018	12.2 mg
Toluene				3 ml

An oven dried Schlenk flask containing a stir bar was charged w/ NaH, evacuated and back filled w/ argon. To this was added ~~+ butyl bromobenzene, Pd_2dba_3, NaOAc, Tol-Binap and 1 ml of toluene.~~ Cyclobutanol and 2 ml of toluene. The mixture was heated for ~10 min at 70°C at which time + butyl bromobenzene, Pd_2dba_3, Tol-Binap, NaOAc and 1 ml of toluene was added. The mixture was heated to 70°C while under argon.

11/26/96 - After 17 hours, took aliquot
MP 6C-II-283-1



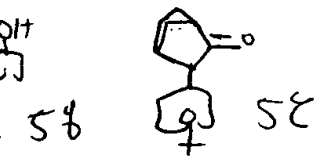


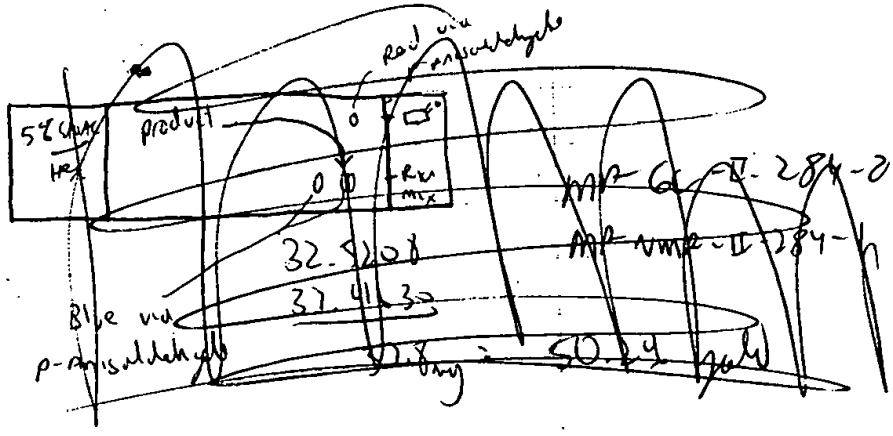
Compound	MW	equiv	mmole	amount
t-Butyl bromberzoate	213.12	1.0	0.5	55mg
Cyclohexanol	86.13	1.2	0.6	81ml
NaOH 60%	23.44	2.0	1.0	40mg
Pd_2dba_3	915.7	0.01	0.005	6.9mg
Tol-Binap	678.74	0.03	0.01	12.2mg
Toluene				3ml

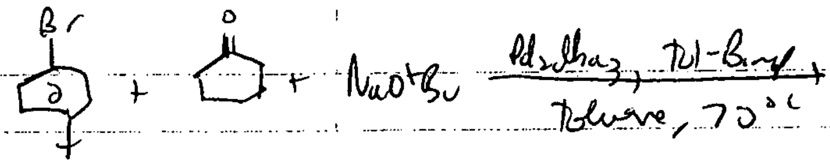
An oven dried Schlenk flask containing a stir bar was charged with NaH, evacuated and back filled with argon. To this was added 2ml of THF and cyclohexanol. The mixture was heated to 70° for 10 min, at which time t-Butyl bromberzoate, Pd_2dba_3, Tol-Binap and 1ml of THF were added. The mixture was heated to 70° while under argon.

11/26/96 - after ~20 hrs, took aliquot

MP-CC-II-284-1

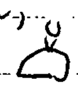




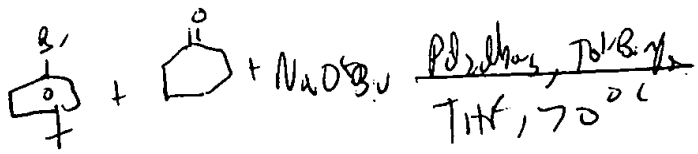


Compound	MW	equiv	mmole	amount	source
t-Butyl Bromobenzene	213.12	1.0	0.5	55 μl	
Cyclohexanone	98.15	1.2	0.6	62 μl	
NaOtBu	96.1	1.3	0.65	65 mg	
Pd_2dba_3	915.7	0.015	0.0075	6.9 mg	
Tol-Binap	678.79	0.036	0.018	12.2 mg	
Toluene				3 ml	

An oven dried Schlenk flask containing a stir bar was charged w/ NaOtBu (from the box), Pd_2dba_3, tol-Binap and 2 ml of Toluene (all under Argon). To this was added t-Butyl Bromobenzene, cyclohexanone and 1 ml of Toluene. The resulting mixture was heated to 70 °C while under argon.

After 6 hours, Took aliquot MP-OC-II-285-1
15%  , 65% prod - others

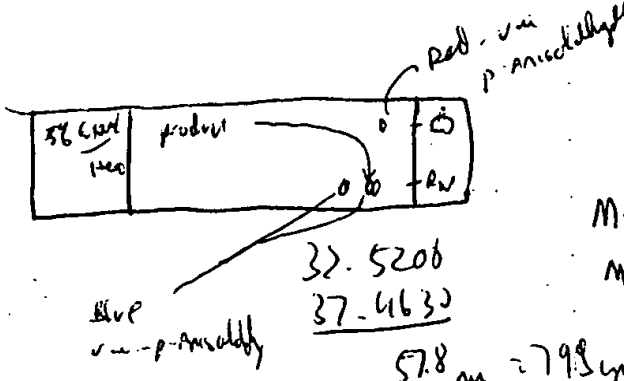
286



Compound	MW	equiv	mmole	amount (should be 87 ml)	room
t-Butyl Bromobenzene	213.12	1.0	0.5 (0.31)	55 ml	
cyclohexanone	98.15	1.2	0.6	62 ml	
NaOtBu	96.1	1.3	0.65	65 mg	
Pd_2dba_3	915.7	0.015	0.0071	6.4 mg	
Tol-Binap	678.74	0.031	0.018	12.2 mg	
THF				3 ml	

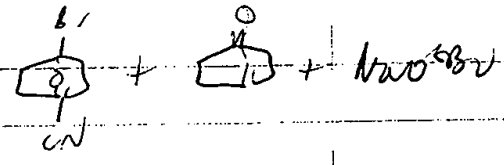
An oven dried Schlenk flask containing a stir bar was charged w/ NaOtBu (Box), Pd_2dba_3 and Tol-Binap (under argon). To this was added THF, t-Butyl Bromobenzene and cyclohexanone. The resulting mixture was heated to 70°C while under argon.

After 6 hrs, TLC chkpt - MP-6(II)-282-1
23% SM, 73% prod, NO SM, NO



MP-6(II)-286-2
MP-NMR-II-286-2

32.5208
37.4633
57.8 mg = 79% yield

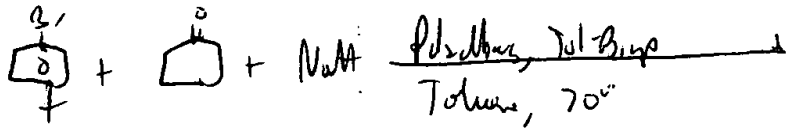


1

Compound	MW	equiv	mmole	amount	source
4-Bromobenzonitrile	182.03	1.0	0.5	91 mg	
Cyclohexanone	98.15	1.2	0.6	62 µl	0.947
NaO^{t}Bu (97%)	96.1	1.3	0.65	65 mg	
Tol-Binap	678.71	0.036	0.018	12 mg	
Toluene				3 ml	
Pd$_2$dba$_3$	915.7	0.0075	0.00375	6.9 mg	

An oven dried Schlenk flask containing a stir bar was charged w/ NaO^{t}Bu (1.3x), Pd$_2$dba$_3$, Tol-Binap and, 1, then 2 ml of Toluene all under argon. To this was added cyclohexanone and 1 ml of Toluene. The mixture was heated to 70° while under argon.

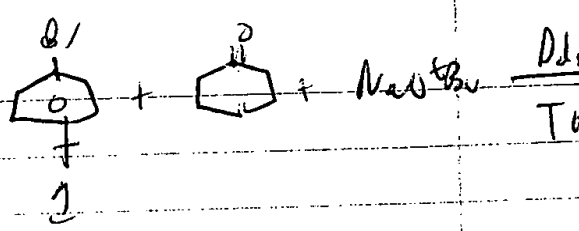
After 4 hours TLC aliquot MP-CC-II-287-1



Compound	MW	equiv	mmole	amount	room
t-Butyl bromobenzene	213.12	1.0	0.5	55 ml	
Cyclohexanone	98.15	1.2	0.6	62 ml	
NaH (60%)	23.99	1.3	0.65	26 mg	
Pd_2dba_3	915.7	0.015	0.0075	6.9 mg	
Tol-Binap	678.74	0.036	0.018	12 mg	
Toluene				3 ml	

An oven dried Schlenk flask containing a stir bar was charged w/ NaH, evacuated and back filled w/ argon 2x. The was added Pd_2dba_3, Tol-Binap, t-Butyl Bromobenzene, cyclohexanone and 3 ml Toluene. The mixture was heated to 70° while under argon

After 6 hours, took aliquot
MR 6(-II-288-1 488 ☝
468 SM

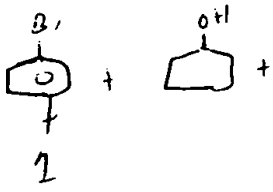


Compound	MW	equiv	mmole	amount	room
1	213.12	1.0	0.5	55 mL	
Cyclohexanone	98.15	1.2	0.6	62 mL	
NaO^{t}Bu	96.1	1.3	0.65	65 mg	
Pd$_2$dba$_3$	915.7	0.015	0.015	6.4 mg	
Tol-Binap	678.74	0.036	0.018	12.2 mg	
THF				3 mL	

An oven dried Schlenk flask containing a stir bar was charged NaO^{t}Bu, Pd$_2$dba$_3$, Tol-Binap evacuated and back filled w/ argon. To this was added 1, cyclohexanone and 3 mL of THF. The mixture was heated to 50°C while under argon

After 3 hours, TLC aliquot 1P-GC-II-289-1
218 ☺, 8.49 om, 67.3% prod

290



2

Start 1:45

Compound	MW	equiv	mmol	amount	source
2	213.11	1.0	0.5	55 mg	
Cyclohexanol	82.12	1.2	0.6	62.4 µl	
NaH (60%)	23.99	2.0	1.0	40 mg	
Bu_4NOAc (95%)	301.5	1.0	0.5	170.8 mg	
Pd_2dba_3	915.7	0.015	0.0075	6.9 mg	
Tol-Binap	678.79	0.036	0.018	12.2 mg	
Toluene				3 ml	

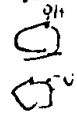
An oven dried Schlenk flask containing a stir bar was charged w/ NaH, Bu_4NOAc (in the box), Pd_2dba_3, Tol-Binap and was stoppered and back filled w/ argon. To this was added 2, cyclohexanol and 3 ml / Toluene. The mixture was heated to 70°C while under argon.

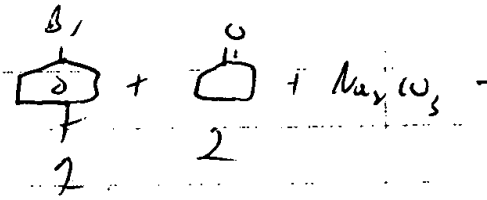
After 3 hrs, Took aliquot. MP-61-II-240-1

55%  , 20%  , 25% ~~SM~~ RT = 2.41

11/30/91

After 22 hrs - Took aliquot MP-61-II-240-1

35%  , 21%  , 37% RT = 2.41



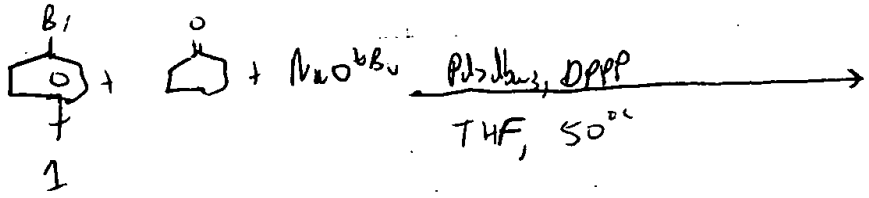
Compound	MW	equiv	mmol	amount
1	213.12	1.0	0.5	55 mL
~~Cyclobutanol~~ 2	18.15	1.2	0.6	62 mL
Na_2CO_3	105.81	1.3	0.65	68.8 mg
$Pd_2(dba)_3$	915.7	0.005	0.0025	6.9 mg
Tol-BINAP	678.71	0.01	0.005	13.2 mg
THF			3 mL	

An oven dried Schlenk flask equipped w/ a stir bar was charged w/ Na_2CO_3, $Pd_2(dba)_3$ and Tol-BINAP. The Schlenk flask was evacuated and backfilled w/ argon. To this was added 1, 2 and 3 mL / THF. The mixture was heated at 70°C while under argon.

after 3 hours, took aliquot - MP-CC-II-291-1
949 ☐, 48% SM no prod.

11/30/16 - after ~ 22 hours, took aliquot
MP-CC-II-291-2 45% ☐, 48% SM no prod.

Start 1:WP

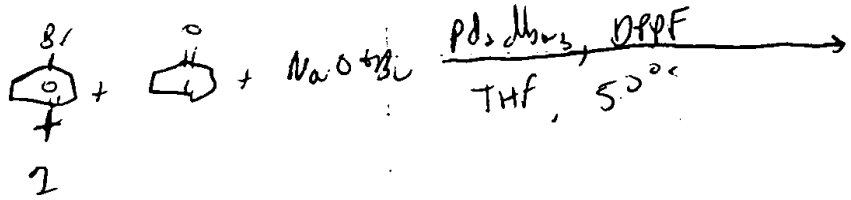


Compound	MW	equiv	mmole	amount	source
1 (177)	213.12	1.0	0.5	90 ml	1.224
Cyclohexanone	98.15	1.2	0.6	62 ml	
NaO^{t}Bu (473)	96.1	1.3	0.65	65 mg	
Pd$_2$dba$_3$	915.7	0.015	0.075	6.9 mg	
DPPP	412.46	0.036	0.018	7.42 mg	
THF				3 ml	

An oven dried schlenk flask was charged w/ NaO^{t}Bu, Pd$_2$dba$_3$, DPPP, evacuated and back filled w/ argon. To this was added 1, cyclohexanone and THF. The mixture was heated to 50°C while under argon

After 3 hrs, TLC eluent - MP-GC-II-242-1
35% [illegible], 65% SM.

12/1/11 - after 24 hrs, TLC eluent MP-GC-II-242-1
15% [illegible], 8% [illegible], 63% SM, ~ 2% yield.



Start rxn

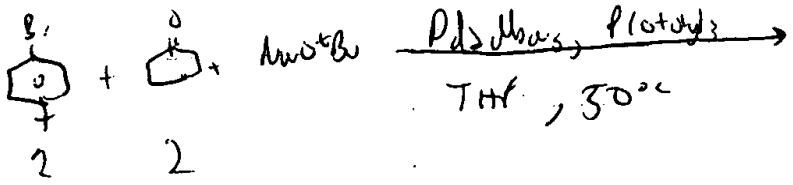
1

Compound	MW	equiv	mmole	amount	source
1 (97%)	213.12	1.0	0.5	90 ml	
Cyclohexanone	98.15	1.2	0.6	62 ml	
NaO^{t}Bu (97%)	16.7	1.3	0.65	65 mg	
Pd_2dba_3	915.7	0.015	0.0075	6.9 mg	
DPPF	554.39	0.036	0.018	10 mg	
THF				3 ml	

An oven dried Schlenk tube was charged w/ NaO^{t}Bu, Pd_2dba_3, DPPF, evacuated and back filled w/ argon. To this was added 1, cyclohexanone, THF and the mixture was heated to 50°C while under argon.

After 3 hours, TLC aliquot MP-61-II-293-1
23% , 3.5% , 46.6% SM, 26% prod.

12/1/98 - After 24 hours, , TLC aliquot MP-61-II-293-2
15.7% , 19.4% , 18% SM, 37.3% prod.



2 2

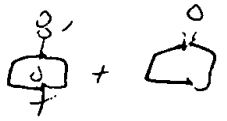
Start 1:00 p

Compound	MW	equiv	mmole	amount	source
1 (97%)	213.12	1.00	0.5	94 mg	
cyclohexanone	98.15	1.2	0.6	62 mg	
NaOtBu (97%)	96.1	1.3	0.65	65 mg	
Pd2dba3	915.7	0.015	0.0075	6.9 mg	
P(otol)3	304.37	0.07	0.035	10.7 mg	
THF				3 ml	

An oven dried Schlenk flask containing a stir bar was charged w NaOtBu, Pd2dba3, P(otol)3 and was evacuated and back filled w argon. 2-Me was added 2 and 2 and THF. The mixture was heated to 50°C while under argon

After 3 hrs, took aliquot - MA-61-II-294-1
6% , 32% , 29% SM, no prod

12/11/96 - After 24 hrs, took aliquot MA-61-II-294-2
5% , 39% , 28% SM, 29% prod.



2 2

Compound	MW	equiv	mmole	amount
1 (97%)	213.12	1.0	0.5	90 mL
Cyclohexanone	98.15	1.2	0.6	62 mL
NaO^{t}Bu (97%)	96.1	1.3	0.65	65 mg
$Pd_2(dba)_3$	915.7	0.015	0.0075	6.9 mg
Tol-BINAP	678.74	0.024	0.012	12.2 mg
THF				5 mL

An oven dried flask was charged w/ NaO^{t}Bu, $Pd_2(dba)_3$, Tol-BINAP and was evacuated and back filled w/ argon. To this was added 1 and 2, THF and the mixture heated to 50°C while under argon

After 3 hrs, took aliquot - mp-6C-II-245-1 25% 31% prod.
44% SM no

12/1/94 - 24 hrs, mp-6C-II-245-2 7.5% 
2% 
86% prod.

46.4443
46.3700

74.3 mg = 65% yield

+  + NaO^tBu $Pd_2(dba)_3$, DPPE, THF, 50°C → 6 at 3:1 dr

2

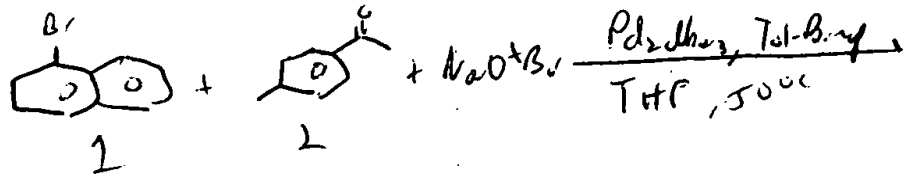
Compound	MW	equiv	mmole	amount	source
1	213.12	1.0	0.5	90 ul	
Cyclohexanone	98.11	1.2	0.6	62 ul	
NaO^tBu	96.1	1.3	0.65	63 mg	
$Pd_2(dba)_3$	915.7	0.015	0.007	6.4 mg	
DPPE	~~534~~ 414.47	0.031	0.016	~~7.2 mg~~ 7.2 mg	
THF				3 ml	

An oven dried Schlenk tube was charged w/ NaO^tBu, $Pd_2(dba)_3$, DPPE and was evacuated and back filled w/ argon. To this was added 1, 2, THF and the resulting mixture heated to 50°C while under argon.

12/12 After 18 hrs - took aliquot MP-61-II-241-1 46 @ 1+
64% SM
no prod.

12/13/96 44 hrs - took aliquot MP-61-II-246-2 7% @ 1+
62% SM
no prod

[redacted]



1 2

Shut 3:45p

260.352

Compound	MW	equiv	mmols	amount	source
1	207.08	1.0	0.5	108ul	
2	134.22	1.2	0.6	80ul	1.00T
NaO^{t}Bu	96.1	1.2	0.65	65mg	
Pd_2dba_3	915.7	0.015	0.0075	6.4mg	
Tol-Binap	678.74	0.036	0.018	12.2mg	
THF				3ml	

12/2/14 – after = 18hrs, Took aliquot – MP-GC-II-301-1

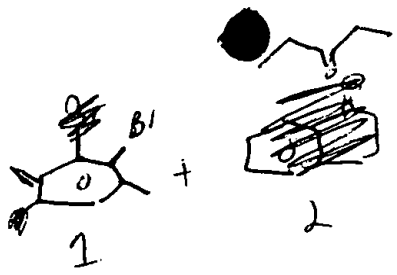
8% naphthalene
35% SM
44% – RT: 9.883

MP-GCMS-II-301-1 MW: 260

12/3/14 – after = 44 hours, Took aliquot MP-GC-II-301-2

4% reduced (naphthalene)
29% SM
59% prod RT: 9.642

43.5043
43.3480
106.3mg? 82% yield

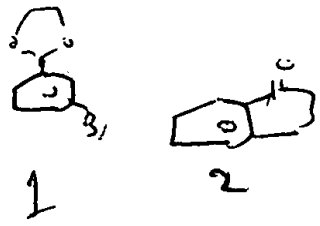


+ K_2OtBu $\xrightarrow[THF,\ 50^\circ]{Pd_2(dba)_3,\ Tol\text{-}BINAP}$ Start 3:00p

Compound	MW	equiv	mmol	amount	
1	185.07	1.0	0.50	67 µl	1.301
2	~~110.1~~ 86.13	1.2	0.60	64 µl	~~1.301~~ 0.814
K_2OtBu	96.1	1.3	0.65	65 mg	
$Pd_2(dba)_3$	915.7	0.015	0.0075	6.9 mg	
Tol-BINAP	617.79	0.032	0.018	12.2 mg	
THF				3 mL	

12/2 After 48hrs - Took aliquot
MP-6C-II-302-1 5% ~~Acid~~ xylene
85% SM

12/3/96 After ~ 44 hours, Took aliquot
MP-6C-II-302-2 4.6% xylene
82.8% SM



1 2

+ NaO^tBu — $Pd_2(dba)_3$, Tol-BINAP, THF, 50°C — Start 3:00 pm

Compound	MW	mmole	equiv	amount	
1	229.03	1.0	0.5	76 mg	1.5 M
2	146.14	1.2	0.6	80 mg	
NaO^tBu	96.1	1.3	0.65	65 mg	
$Pd_2(dba)_3$	915.7	0.015	0.0075	6.9 mg	
Tol-BINAP	678.79	0.032	0.016	12.1 mg	
THF				3 mL	

12/21/96 – after 18h, Task aliquot — MA 6C-II-303-1
35% RT = 3.864
62% RT = 11.260

12/31/96 – after 44h Task aliquot — MA 6C II 303-2